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ALLERGIC SKIN REACTIONS IN PNEUMONIA TO TYPE STRAINS OF PNEUMOCOCCI *

STUDIES IN PNEUMONIA, V

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Allergic skin reactions in pneumonia have recently been studied during the course of immunologic investigations in this disease. Clough,¹ in 1915, studied allergy in pneumonia with the dried and ground residue of 18-hour extracts of washed pneumococci before and after precipitation with absolute alcohol. Ophthalmic, cutaneous, and intracutaneous tests with these extracts on persons with pneumonia and controls yielded varying and inconstant results attributable to the irritant qualities of the extracts, so that Clough was of the opinion that it is not possible to demonstrate a condition of hypersensitiveness to pneumococcus protein in patients with pneumonia by these tests.

In the autumn of 1915, we began the study of allergic reactions in pneumonia with suspensions of washed and heat-killed pneumococci, our object being to determine whether such emulsions were suitable for these tests and whether a condition of skin hypersensitiveness to pneumococcus protein develops in pneumonia, and if so, to apply anaphylactogens prepared of different types of pneumococci in a study of the specificity of allergic reactions in this disease as controlled by a bacteriologic diagnosis of the type or types of pneumococci found in the sputum. During the course of this investigation Weil and Torrey² reported the results of their work using Dale's method and an extract of pneumococci prepared by autolyzing the cocci in distilled water for 2 hours at 37 C. and heating at 60 C. for 1 hour. Weil and Torrey found that the blood of persons suffering with pneumonia contains a sensitizing antibody during the course of the disease, but none after the crisis. These anaphylactic reactions were found more general for

* Received for publication November 27, 1916.

¹ Bull. Johns Hopkins Hosp., 1915, 26, p. 37.

² Jour. Exper. Med., 1916, 23, p. 1.

the whole pneumococcus group than has been found to be the case with agglutination and protection tests. Weil³ injected from 0.1 to 0.2 c.c. of this extract into the skins of persons suffering with pneumonia and found no reactions during the course of the disease while "after subsidence a considerable percentage presented a reaction."

METHOD OF STUDY

Intradermal skin tests with anaphylactogens corresponding to Types I, II, and III were conducted in a group of persons suffering with lobar pneumonia both before and after the crisis, in whom a bacteriologic diagnosis of the type or types of infecting pneumococci present in the sputum had been made by the agglutination test; also in a number of healthy persons and those suffering with various chronic ailments not referable to the respiratory system.

Preparation of the Anaphylactogens.—Pure cultures of pneumococci highly virulent for mice and rabbits and belonging to serologic types I, II, and III, were grown in flasks of specially prepared dextrose broth for 48 hours; the cocci of each type were then removed and washed twice with sterile normal salt solution by centrifugation in order to remove toxic substances present in the medium. The three lots of washed cocci were then suspended in sterile salt solution, shaken mechanically, and the emulsion diluted with sufficient salt solution to make about 2 billion cocci to the cubic centimeter. Each emulsion was then heated in a water bath at 60 C. for 1 hour, cultured for sterility, and preserved with 0.2% tricresol.

Tests and Reactions.—In conducting the tests 0.1 c.c. of each emulsion was injected intracutaneously. The three injections were made at the one time in each patient.

All reactions were read 48 hours after injection. During the first 24 hours the majority of persons, both controls and those suffering with pneumonia, showed a narrow zone of hyperemia about each injection which had largely subsided in 48 hours, except in those whose reactions were interpreted as positive. Areas of erythema less than 1 c.c. in diameter and even accompanied by a small papule which regularly disappeared in 72 hours, were regarded as possibly due to irritation and negative reactions.

Positive reactions were those marked by the formation of a definite papule with an area of erythema greater than 1 c.c. in diameter and accompanied by slight edema. These reactions persisted for from 4 to 5 days and gradually disappeared. Pustular reactions did not occur in any instance.

There were no subjective symptoms beyond slight burning pain within a few hours after injection.

RESULTS WITH HEALTHY PERSONS AND THOSE SUFFERING WITH DISEASES OTHER THAN PNEUMONIA

A large number of tests with the three anaphylactogens were made on healthy persons and those suffering with various chronic ailments not involving the chest. In all instances the skin reactions were regarded as negative and uninfluenced by the presence of various types

³ Ibid., p. 11.

of pneumococci in the upper air passages. As previously stated, many of these persons presented mild reactions of erythema which disappeared in 48 hours, but these were no greater in our experience than those observed to follow other cutaneous reactions as in the luetin test. For this reason we believe that the anaphylactogens as prepared were free to a large extent of toxic or irritant substances.

RESULTS IN PERSONS WITH PNEUMONIA

The results observed in a group of 20 cases are shown in the accompanying table.

TABLE 1
ALLERGIC SKIN REACTIONS IN PNEUMONIA PATIENTS

No.	Age (yr.)	Clinical Diagnosis	Type of Pneumonia	Day of Disease	Relative to Crisis	Allergic Reactions		
						Type I	Type II	Type III
1	45	Bronchopneumonia* Double lobar	None present	10	Lysis	—†	—	—
2	34		II	5	Before	—	—	—
3	49		II	27	Lysis	—	—	—
4	23		I	10	Lysis	—	—	—
5	19		I	13	2d day after	+	—	+
6	33	Lobar pneumonia†	Not examined	26	Lysis	—	—	—
7	34		I and II	8	Before	—	—	—
8	34		IV	10	3d day after	—	—	+
9	40		IV	7	Same day	—	—	—
10	35		I and III	Unknown	9th day after	—	—	+
11	58		II	3	Before	—	—	—
12	35		II	13	Before	—	—	—
13	36		I and II	39	Lysis	—	+	+
14	51		I and II	3	Before	—	—	—
15	35		I	32	23d day after	—	—	—
16	23		I and II	24	16th day after	—	—	—
17	28		Not examined	14	5th day after	—	—	—
18	31		I and II	12	5th day after	—	+	—
19	23		I and IV	9	4th day after	+	—	—
20	32		IV	9	Before	—	—	—

* *M. catarrhalis*.

† No. 3 developed empyema. Nos. 6 and 13 doubtful.

‡ — = negative skin reaction. + = positive skin reaction.

As shown in the table, of 17 cases in which a diagnosis of the pneumococci present in the sputum had been made, the following types were found: Type I (alone) in 3 cases; Type II (alone) in 4 cases; Type IV (alone) in 3 cases; Types I and II in 5 cases; Types I and III in 1 case; and Types I and IV in 1 case.

Of 19 cases regarded clinically as lobar pneumonia, 6 or 30% gave positive reactions with one or more of the anaphylactogens.

In all instances the positive reactions occurred after the crisis (in one case, No. 13, there was no crisis and the positive reactions occurred on the 39th day of the disease). In our series the earliest reaction was observed on the 10th day of the disease and the 3rd after the crisis.

The positive skin reactions did not correspond strictly to the types of pneumococci found in the sputum, altho we may have overlooked other types in the sputum. Case 5 showed Type I in the sputum and reacted in the skin to the protein of Types I and III; Case 8 showed Type IV in the sputum and reacted to Type III; Case 10 showed Types I and III in the sputum and reacted to Type III; Case 13 showed Types I and II in the sputum and reacted to Types II and III; Case 18 showed Types I and II in the sputum and reacted to Type II; Case 19 showed Type I and IV and reacted to Type I (Type IV not included in the skin tests).

Further studies must determine how long this condition of hypersensitiveness persists and its relation to immunity in pneumonia.

As the reactions are not observed until after the crisis and as they apparently do not occur according to the types of pneumococci found in the sputum, these tests possess no appreciable practical value.

SUMMARY

Allergic reactions were observed in 30% of a series of cases of lobar pneumonia following the intradermal injection of washed and heat-killed pneumococci.

True reactions were not observed among normal persons or those suffering with various chronic diseases, and the presence of pneumococci in the upper air passages during health apparently does not sensitize in so far as this condition is detectable by skin tests.

All reactions occurred after the crisis or after the infection had been present over a prolonged period.

There was no constant relation between reactions to the protein of various types of pneumococci and the types found in the sputum. It is probable that the allergic reactions to pneumococcus protein are of a more general character than the agglutination reactions.